# Neuroinformatics and the BIRN

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# Building on Neuroinformatics Initiatives

- HBP
- LINC
  - PedDB, NIF, SemWeb, NCBCs, BIRN
     IMAG/MSM, CRCNs, NIfTI, ADNI, KEBR,
     INCF
- New initiatives under the Blueprint







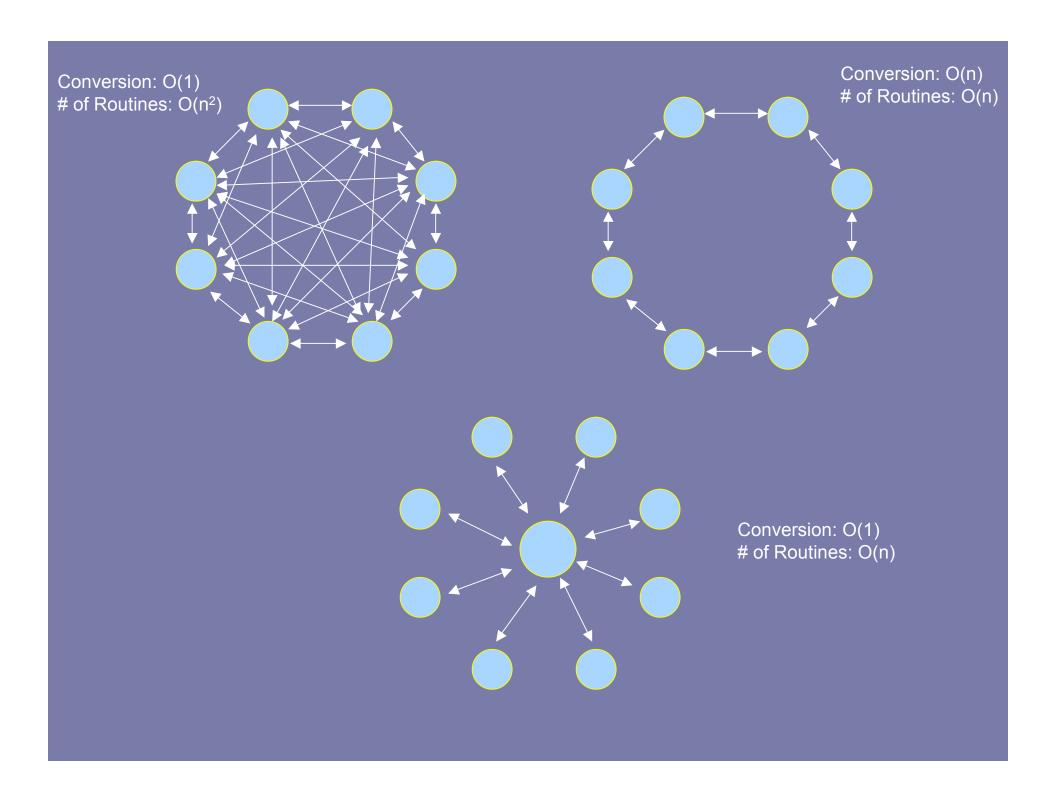




## Tying together communities

Formats, Schemas, Pipelines, and Semantics





# THE ASCENT OF THE INTERNET

Decades after its birth, the Net is finally blossoming into a uniquely social medium



### ONE-TO-ONE

Starting in the 1980s, e-mail became the first popular application on the Internet. Best for connecting two people, just like traditional mail, it has suffered with the advent of widespread spam.



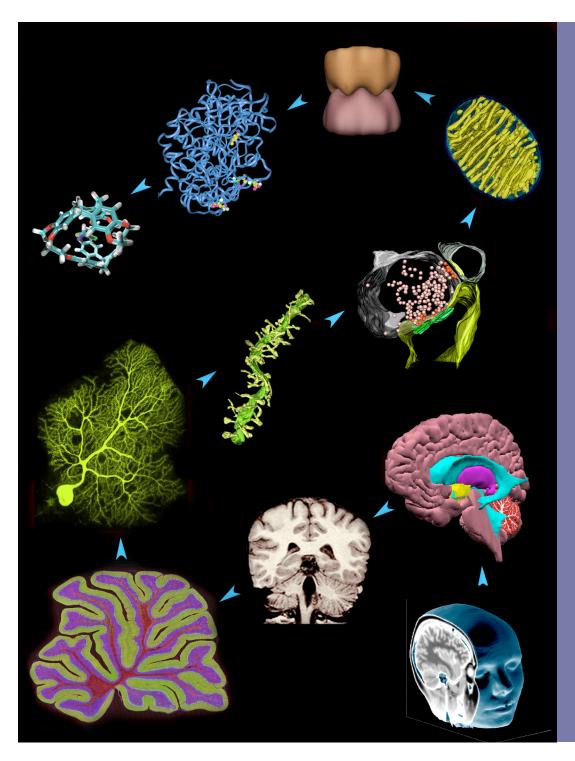
### ONE-TO-MANY

With the emergence of the Web browser in 1993, the World Wide Web developed into a broadcast medium. But television still plays that game much better.



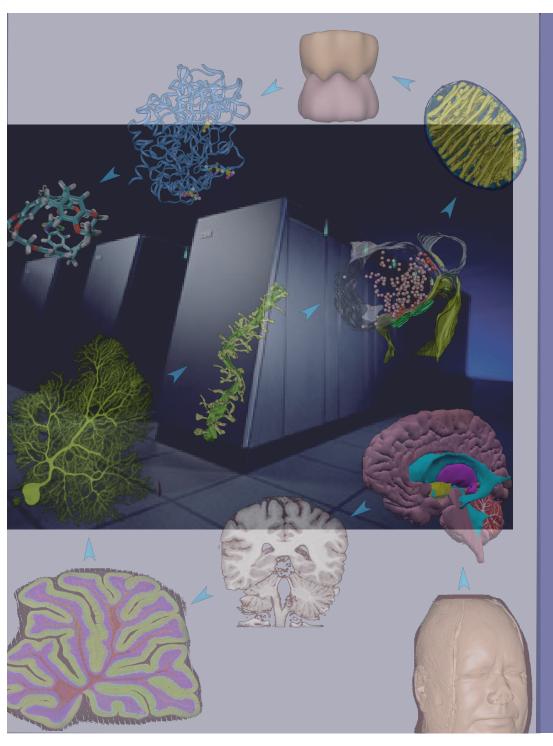
### MANY-TO-MANY

File-sharing, blogs, and social networking services are connecting masses of people simultaneously. Their collective efforts are spawning new services, including online encyclopedia Wikipedia and free Net phone network Skype.



### **BIRN Mission**

Develop an infrastructure that enables science that would not be possible or likely within the confines of a single laboratory. Ensure that the infrastructure is accessible, adoptable, and scalable in such a way that it can be used by anyone to realize largescale cross-institutional scientific projects. The infrastructure should support unique developments and discoveries leading ultimately to improved healthcare.



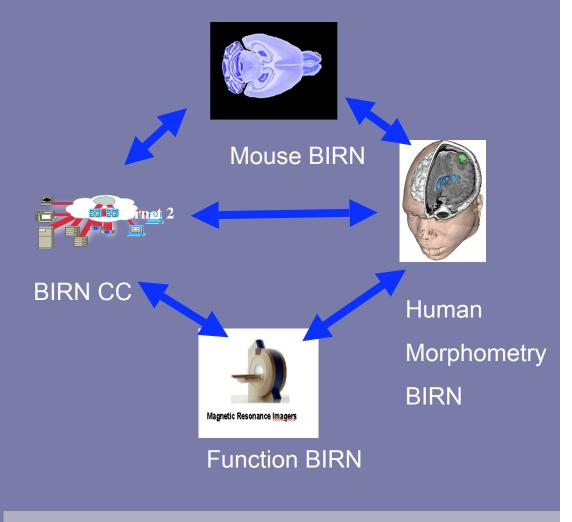
### **Secondary Goal**

•Create an environment where a large group of computer scientists and information technology professionals from around the world can push their science and advance their careers while making contributions to biomedical research.

## BIRN Collaboratory Today



Enabling collaborative research at 28 research institutions comprised of 37 research groups.



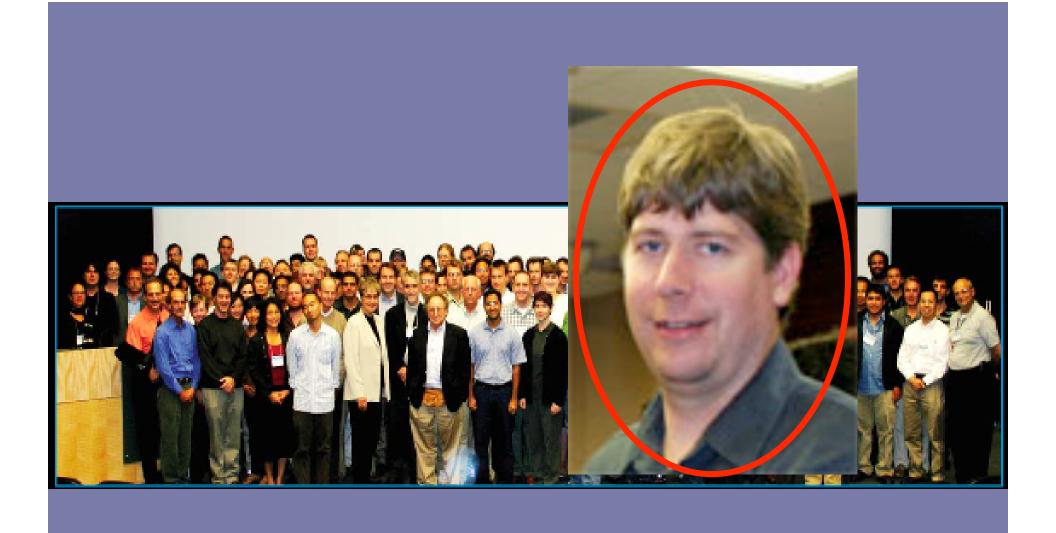


It will no longer matter where data, instruments and computational resources are located!



Old age and treachery will overcome youth and skill.

- Gary Glover's email tag line



Old scientists do not change their minds; they simply die, and new and younger scientists come along for whom the new paradigm is not so threatening.

- Max Planck

### **BIRN Contributions**

Taking advantage of the multi-site perspective

- Multiple manufacturers
- Tighter feedback loops
- Multiple modalities
- Extensibility



Function BIRN Stability Phantom QA Procedures - The Quality Assurance scans are performed on a routine basis. They are used to verify and measure the scanner stability during a typical fMRI scanning sequence. The scans are performed on a 17cm spherical phantom filled with an agar gel. The scans consist of 200 separate image volumes captured over roughly a 10 minute interval. Post acquisition analyses consist of

BIRN - Downloads

XML-Based Clinical Experiment Data Exchange Schema (XCEDE) - This schema provides an extensive metadata hierarchy for describing and

XCEDE SPM Toolbox - A toolbox for SPM was created to capture the results from activation maps using the XCEDE schema. The toolbox supports both SPM99 and SPM2 statistical structures and has been tested on SUN, LINUX, and Microsoft Windows operating systems, The toolbox has been used to capture PET and fMRI analysis results and the associated analysis model specifications.

BXH/XCEDE Tools - A suite of tools designed to read, write and manipulate XML descriptors using the BXH or XCEDE schemas. These descriptors are "wrappers" of the original, unadulterated image data files, and provide a standard interface to image data and other metadata extracted from the image headers. Also provided are tools to create and use XML "event" descriptors, for representing stimulus presentation and other time-based data.

Human Imaging Database: The Human Imaging Database (HID) has been developed to address the problems associated with managing the increasingly large and diverse datasets collected throughout clinical and imaging communities. The HID is an extensible database management system that is comprised of three core components:

- Human Imaging Database Schema The HID Schema has been designed so that it can be customized and extended to contain relevant information from any particular sites needs without requiring modification to the schema itself. This information can consist of data concerning the research subjects used in an experiment, subject assessments and demographics, the experimental data collected, the experimental protocols used and any annotations or statistics (metadata) normally included with an experiment or study.
- . Clinical Assessment Layout Manager This application works in conjunction with the HID and facilitates the preparation and incorporation of on online clinical assessment entry forms.
- Human Imaging Database Graphical User Interface The HID user interface allows for the management of research subjects and experiments.

### **Data Analysis**

Mouse Brain Atlas Tool (MBAT) - The Mouse BIRN Atlasing Tool is designed to view multiple types of multiscale data, access and guery databases associated with the mouse BIRN, and process some of these data types.

Link

Remote Scripting with IFRAME

BT URLS

Mouse 3D Atlas - An atlas based on a magnetic resonance microscopy (MRM) image diffusion-weighted in the Z-direction acquired from a normal, 100-day old male C57BL/6J mouse. The atlas is comprised of a diffusion-weighted image volume, a label volume, a mask volume, and a label index.

Mouse DTI Atlas - An atlas of developing mouse brains from embryonic and adult mouse brain images. The images were acquired using three dimensional diffusion tensor magnetic resonance microimaging technique. The atlas consists of a viewing software and diffusion tensor MR images from E14, E15, E16, E17, E18 and adult mouse brains.

Mouse Shiverer DTI - High-resolution (80um isotropic) contrast-enhanced diffusion tensor data was acquired from six background control (C3HeB) and six dysmyelinating shiverer (C3Fe.SWV shi/shi) mouse brains. The data consists of nominally unweighted and diffusion weighted images with optimized icosahedral sampling.

Cerebellum Large Scale Mosaic - Large scale multiphoton microscopy mosaic image from cerebellum of C57BL/6H normal mouse. A high resolution multiphoton microscopy mosaic image of a cerebellar distribution of cell bodies (Hoescht 33342; blue) and alpha-synuclein (green) from a non-transgenic animal.

Hippocampus Large Scale Mosaic - Large scale multiphoton microscopy mosaic image from hippocampus of C57BL/6H D-line transgenic mouse overexpressing alpha-synuclein. A high resolution multiphoton microscopy mosaic image of distribution of cell bodies (Hoescht 33342; blue) and alpha-synuclein (green) from a D-line transgenic animal overexpressing alpha-synuclein under the PDGF promoter.

Mouse Common Specimen - The Common Specimen Study involved imaging a single fixed specimen using MRM from Duke's CIVM, Diffusion Weighted MR from Caltech's Beckman Institute, and Optical Histology and Staining from UCLA's LONI. UCSD's NCMIR performed Multiphoton Microscopy using tissue from an animal of the same strain.

#### Human

Open Access Structural Imaging Series - The Open Access Structural Imaging Series (OASIS) is a series of structural MRI data sets that is being made publicly available for study and analysis. This initial data set consists of a cross-sectional collection of 400 subjects covering the adult life span. For each subject, 3 or 4 individual T1-weighted MRI scans obtained in single scan sessions are included. The subjects are all right-handed and approximately equally divided by gender. 100 of the included subjects over the age of 60 have been diagnosed with very mild to mild dementia of the Alzheimer's type (DAT). Additionally, a reliability data set of images obtained from 20 of the non-demented subjects on a subsequent visit are included.

Structural MRI Calibration Data - Structural MRI data from 5 healthy volunteers scanned multiple times on multiple sites having different 1.5T systems (Siemens, GE, Piker). For each subject, four multi-spectral structural scans were obtained in a single scan session, from which tissue proton density and T1 maps can be derived. These data was acquired to investigate various metrics of within-site and across-site reproducibility.

Diffusion MRI Calibration Data - This database contains structural and diffusion MRI data from two healthy volunteers that were scanned multiple times on a 1.5T Philips system to investigate reproducibility of diffusion-derived metrics, such as fractional anisotropy maps.

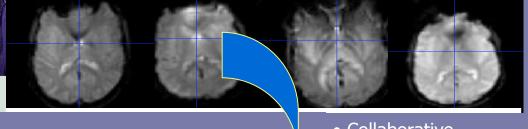
Function BIRN Phase I Traveling Subjects Dataset - The Phase I subject pool consisted of five right-handed healthy male subjects. These subjects traveled to each FBIRN site and were tested twice at each site on successive days. Subjects were scanned in each MRI scanner at least twice using the calibration and cognitive protocols to produce a dataset to measure intersite, intersubject, and intersession variance.

## FBIRN Traveling Humans Study

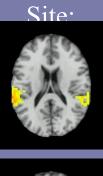


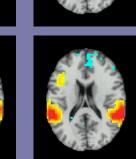
MINN

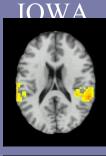
- Subjects traveled around the country to be scanned at all FBIRN sites.
  - Big differences were seen in images from different scanners for a single subject.

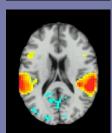


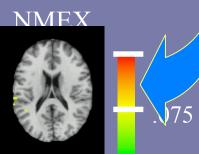
Before After

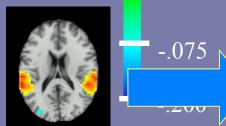












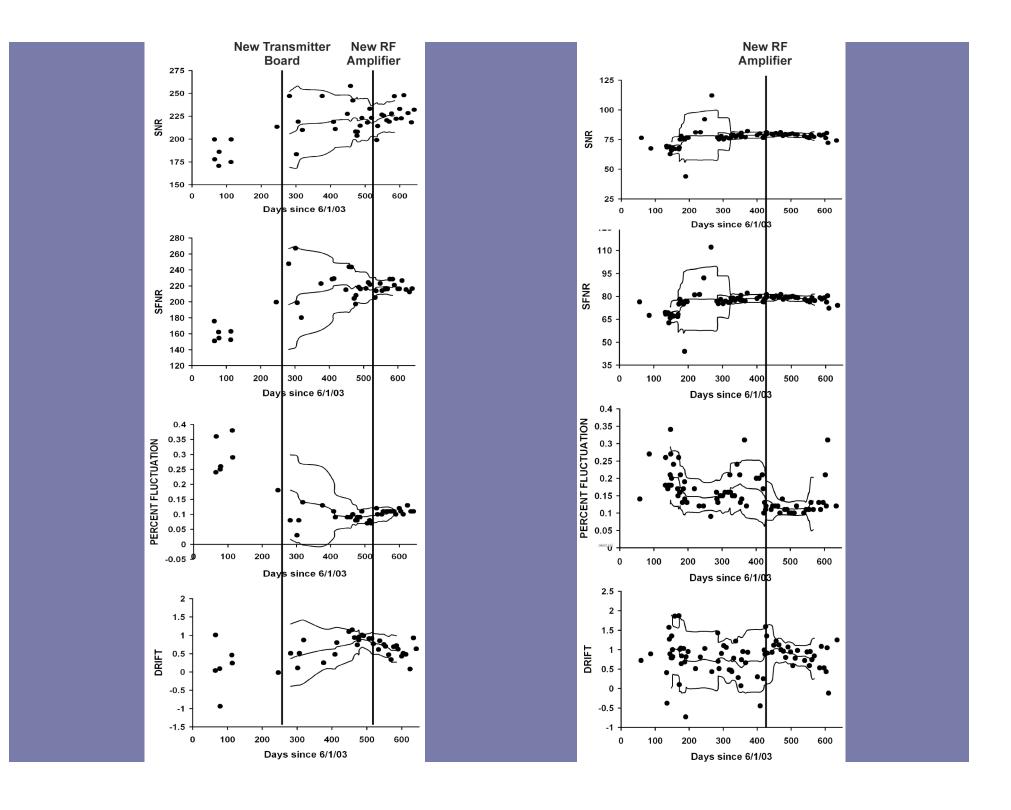
- Collaborative efforts around scanner calibration, task protocols, and processing pipelines greatly reduced intersite variability.
  - These techniques will enable combining of images of disease states collected around the world.

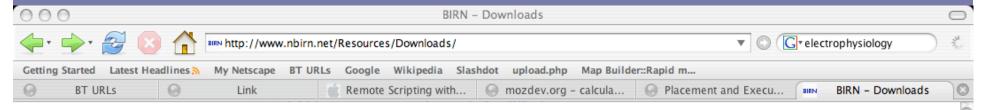
### **BIRN Contributions**

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Center	Abbreviation	Field Strength	Manufacturer	RF coil type	Functional sequence
Brigham & Women's	BWHM	3.0T	GE	GETR Research Coil	EPI
Duke/UNC	D40T	4.0T	GE Nvi LX	TR quadrature head	Spiral
Duke/UNC	D15T	1.5T	GE Nvi LX	TR quadrature head	Spiral
University of lowa	IOWA	1.5T	GE Signa CV/i	TR quadrature head	EPI
Mass. General Hospital	MAGH	3.0T	Siemens Symphony Trio	TR quadrature head	EPI -Dual Echo
University of Minnesota	MINN	3.0T	Siemens Symphony Trio	TR quadrature head	EPI
University of New Mexico	NMEX	1.5T	Siemens Sonata	RO quadrature head	EPI
Stanford University	STAN	3.0T	GE CV/NVi	Elliptical quadrature head	Sp iral in/out
University of California, Irvine	UCIR	1.5T	Philips/Picker	RO quadrature head	EPI
University of California, San Diego	UCSD	1.5T	Siemens Symphony	TR quadrature head	EPI





**B0** and eddy current correction code for diffusion MRI - Software tool (excecutable and source code) and recommendations for acquisition protocols to correct distortions in diffusion MR images that are generated by main magnetic field inhomogeneities and eddy current generated from the direction-dependent diffusion encoding gradients.

**Defacer for Structural MRI** - This package contains an algorithm for removing identifiable facial features (eyes, nose, and mouth). This algorithm, which is still under the validation phase, locates the subject's facial features and removes them without disturbing brain tissue. The algorithm was devised to work on T1-weighted structural MRI; it produces a defaced structural image, and an image of the applied mask. The code mri\_deface produces a facial mask. The code mri\_mask is then used to apply the mask to the original volume, resulting in a defaced structural image. For images in other modalities, the mask can be co-registered to the image before application.

**Gradient non-linearity distortion correction** - The goal of this software is to provide a 3D correction of image distortions in MRI data due to non-linearity of the magnetic fields from the imaging gradient coils.

#### Data

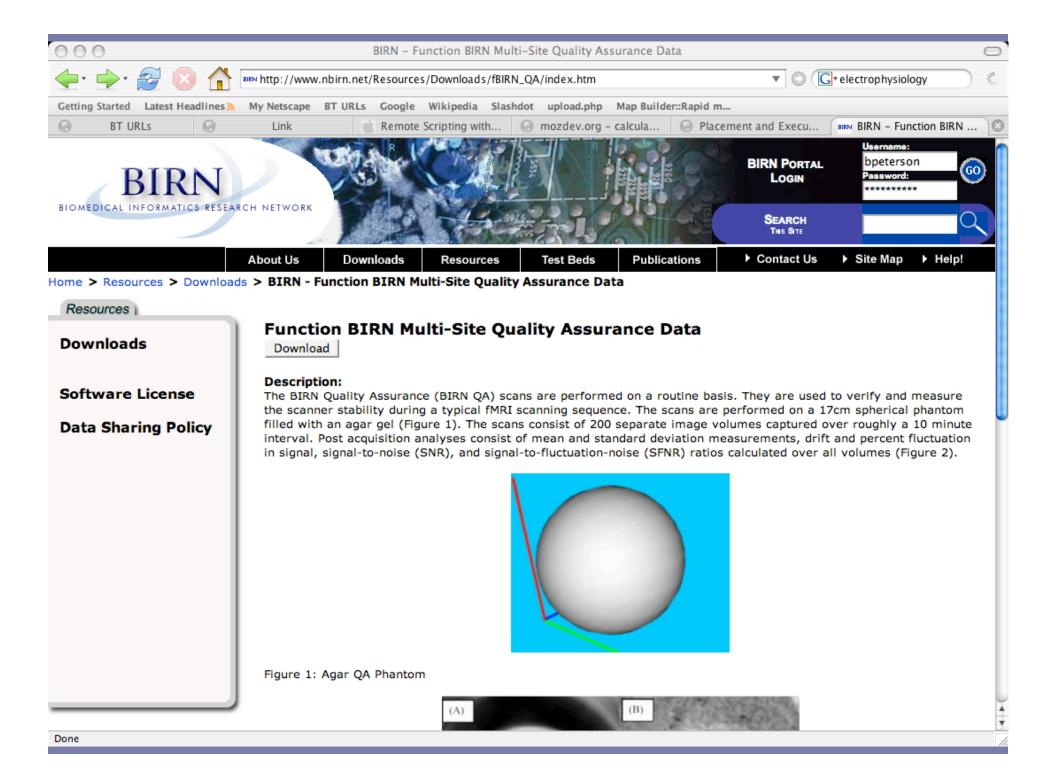
#### Calibration

Function BIRN Multi-Site Quality Assurance Data - These Quality Assurance scans are performed on a routine basis. They are used to verify and measure the scanner stability during a typical fMRI scanning sequence. The scans are performed on a 17cm spherical phantom filled with an agar gel. The scans consist of 200 separate image volumes captured over roughly a 10 minute interval.

#### Mouse

Mouse 3D Atlas - An atlas based on a magnetic resonance microscopy (MRM) image diffusion-weighted in the Z-direction acquired from a normal, 100-day old male C57BL/6J mouse. The atlas is comprised of a diffusion-weighted image volume, a label volume, a mask volume, and a label index.

Mouse DTI Atlas - An atlas of developing mouse brains from embryonic and adult mouse brain images. The images were acquired using three dimensional diffusion tensor magnetic resonance microimaging





### FBIRN Stability phantom QA procedures:

By G. H. Glover, Stanford University and FBIRN

The Quality Assurance scans must be performed on a routine basis. They are used to verify scanner stability. Analysis can be performed locally.

### A. Stability Phantom protocol

The stability (agar) phantom consists of two parts: The spherical phantom itself and the agar material inside. The agar phantom recipe follows this protocol.

The agar phantom (17 cm sphere filled with agar gel) should be scanned at least once/week. The scan is performed with the head coil that is used for the fMRI scans. The scan protocol should be identical to that employed for the human fMRI scans except a straight axial scan plane is used. A consistent protocol should be used so that deviations from the scanner's usual performance can be detected.

The sequences used originally were:
Pulse sequence = EPI or Spiral GRE
Scan plane = axial
FOV = 22 cm
28 slices, 4mm thick, 1 mm gap
TR = 2000ms
TE = 30ms (3T/4T), 40ms (1.5T)
FA = 90 degrees
BW = ±100 kHz
64x64 matrix, 1 shot
200 time frames (volumes)

(A TR of 3000 ms with 5 mm slices and no gap was also used by the FBIRN in the original multisite stability phantom dataset.)

With reference to Fig. 1, the Matlab analysis software ga calc fbirn m reads 200 images from a central slice (slice # 18) time series and provides readings of RMS stability, drift, mean value, SNR,

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### Goals

## Tools to share and mine multi-scale structural and functional mouse brain data

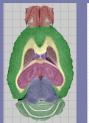
- Digital Atlases
- Integrate Gene Expression Efforts
- Automated Image Processing
- Integrated Interface Applications
- Focus on: Neurodegenerative Diseases

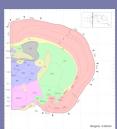


# Designing this Data Integration Framework

Spatially Coregistered Images in Database

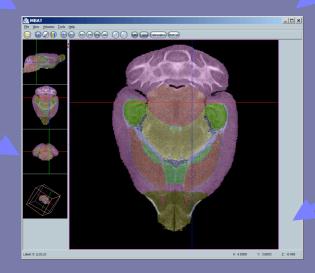
Coregistered Atlas Modules







MOUSE BIRN ATLASING TOOLKIT



Ontologies



Web Based Resources







### **MBAT Manual**

### **HOW TO SETUP AND RUN MBAT**

#### Java

MBAT requires Java version 1.4 or greater. Download and install the appropriate version for your computer at:

http://java.com/en/download/index.jsp

If you wish to use the 3D surface viewing tool, you must have Java 3D installed on your computer:

https://sdlcweb1d.sun.com/ECom/EComActionServlet;sessionid=2938D70F6EFC1B CFC580FC5E18288275

The Runtime version should be fine for most people, while the choice between the DirectX and OpenGL version may depend on your video card.

#### Architecture

MBAT is written in Java in order to be platform independent. It has been tested on Irix, Linux, Macintosh, and Windows operating systems.

#### Launching MBAT

On most machines, double-clicking on MBAT.jar will launch the program. If that does not work, then execute "java –jar MBAT.jar" from the command line interface.

MBAT has command line options and supports loading files at startup. Execute "java –jar MBAT.jar –h" for a list of available options.

The zero coordinate in MBAT is the bregma point, a landmark visible on the skull. The default position of the crosshairs is located at this point, so the horizontal (xz) view may appear to be empty, but this is simply because there is no image data in this horizontal plane. Moving the crosshairs down in one of the other views will show any horizontal data at that point.





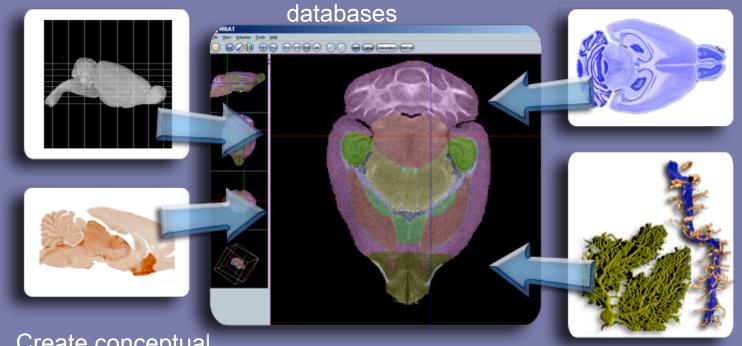
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# Mouse BIRN Data Integration Framework

1. Create multimodal



2. Create conceptual links to a shared ontology

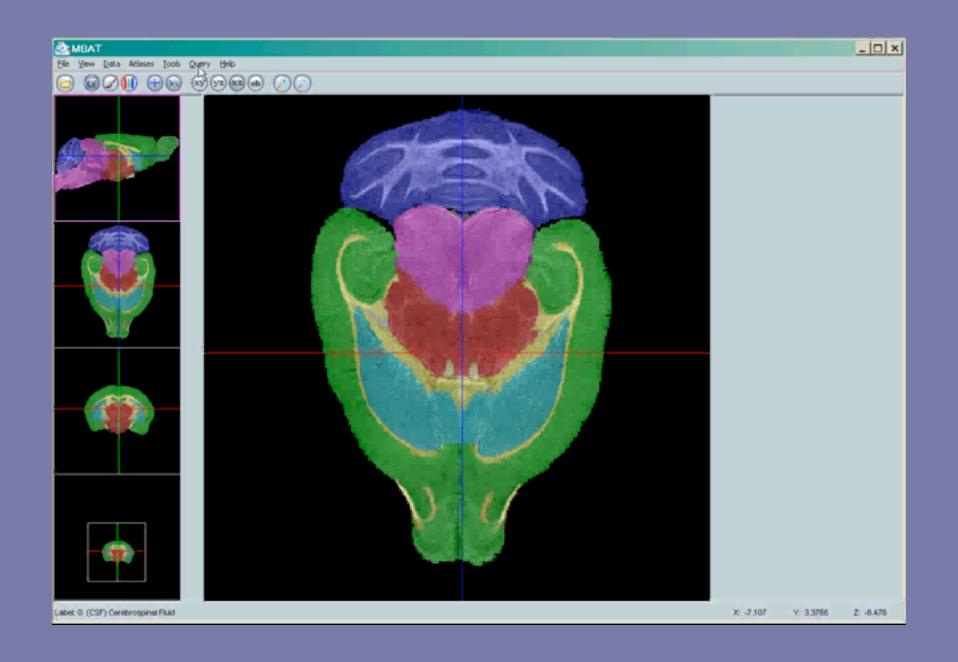
3. Situate the data in a common spatial framework

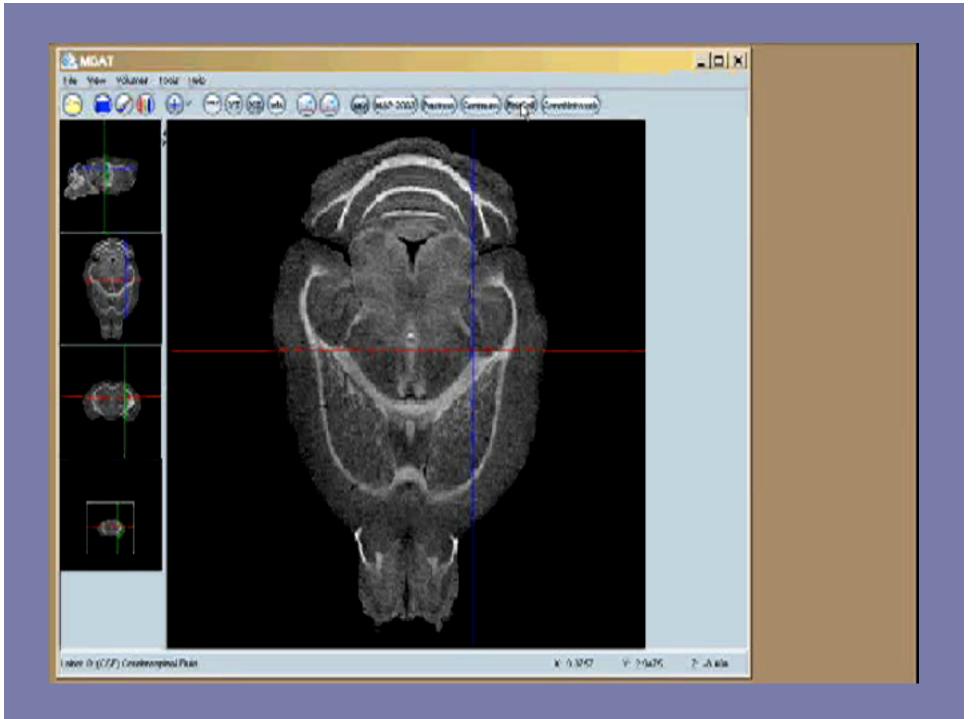
4. Use mediator to navigate and query across data sources

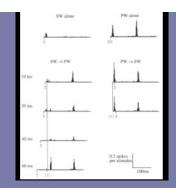
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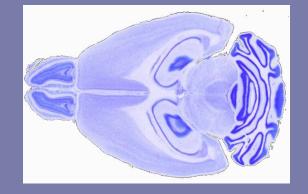
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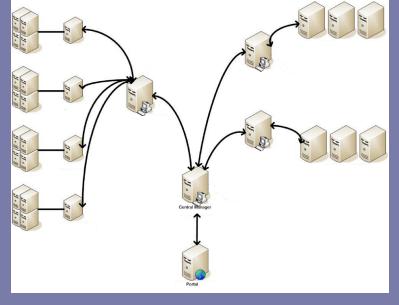


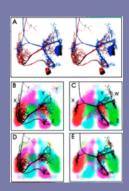


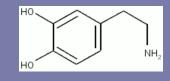


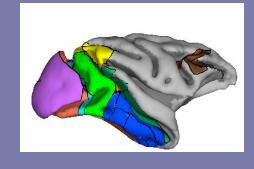


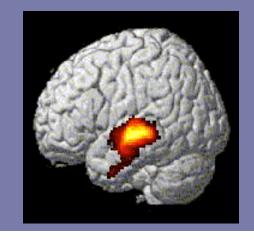


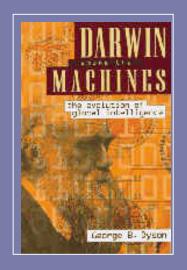












If bandwidth begins to match the internal processing power of individual nodes in a communications network, individuality begins to merge ...

"If we were ever to put all our brains together in fact, to make a common mind the way the ants do," warned Lewis Thomas, "it would be an unthinkable thought, way above our heads."

Distributed intelligence, or composite mind is a nebulous idea. On the other hand, we do not know of any intelligence that is *not* distributed, or any mind that is *not* composite.

- George Dyson Darwin among the Machines (1998) see Max Planck quote



Biology is an information science.
- Sydney Brenner

## MILESTONES IN SCIENTIFIC COMPUTING

#### PRE 1960s>>

1946 ENIAC, widely thought of as the first electronic digital computer, is formally unveiled. Designed to compute ballistics during the Second World War, it performs calculations in a variety of scientific fields including randomnumber studies, wind-tunnel design and weather prediction. Its first 24-hour forecast takes about 24 hours to do.



**1951** Marvin Minsky, later of the Massachusetts Institute of Technology (MIT), builds SNARC, the first machine to mimic a network of neurons.

**1954** John Backus and his team at IBM begin developing the scientific programming language Fortran.

1956 Building on earlier experiments at the University of Manchester, UK, and elsewhere, MANIAC at the Los Alamos National Laboratory in New Mexico becomes the first computer to play a full game of chess. In 1996, IBM's Deep Blue computer will defeat world chess champion Garry Kasparov.



**1959** John Kendrew of the University of Cambridge, UK, uses computers to build an atomic model of myoglobin using crystallography data.

#### 1960s>>

1962 Charles Molnar and Wesley Clark at MIT's Lincoln Laboratory design the Laboratory Instrument Computer (LINC) for researchers at the National Institutes of Health. It is the first lab-based computer to process data in real time.



**1963** In California, the Rancho Arm becomes the first artificial robot arm to be controlled by a computer.

**1966** Cyrus Levinthal at MIT designs the first program to represent and interpret protein structures.

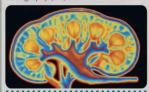
**1967** ARPANET — the predecessor of the Internet — is proposed by the US Department of Defense for research networking.

**1969** Results of the first coupled ocean-atmosphere general circulation model are published by Syukuro Manabe and Kirk Bryan, paving the way for later climate simulations that become a powerful tool in research on global warming.

#### 1970s>>

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**1971** Computing power shows its potential in medical imagery with a prototype of the first computerized tomography (CT) scanner.



**1971** The Protein Data Bank is established at Brookhaven National Laboratory in Upton, New York.

**1972** Hewlett Packard releases the HP-35, the first hand-held scientific calculator, rendering the engineer's slide rule obsolete.

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**1976** At Los Alamos, Seymour Cray installs the first Cray supercomputer, which can process large amounts of data at fast speeds.



#### 1980s>>

1983 Danny Hillis develops the Connection Machine, the first supercomputer to feature parallel processing, It is used for artificial intelligence and fluid-flow simulations.

**1985** After receiving reports of a lack of high-end computing resources for academics, the US National Science Foundation establishes five national supercomputing centres.

**1989** Tim Berners-Lee of the particle-physics laboratory CERN in Geneva develops the World Wide Web—to help physicists around the globe to collaborate on research.



### 1990s>>

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1990 The widely used bioinformatics program Basic Local Alignment Search Tool (BLAST) is developed, enabling quick database searches for specific sequences of amino acids or base pairs.

**1996** George Woltman combines disparate databases and launches the Great Internet Mersenne Prime Search. It has found nine of the largest known Mersenne prime numbers (of the form  $2^n$  – 1), including one that is 9,152,052 digits long.

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1996 Craig Venter develops the shotgun technique, which uses computers to piece together large fragments of DNA code and hastens the sequencing of the entire human genome.

**1998** The first working quantum computers based on nuclear magnetic resonance are developed.

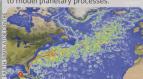
#### 21st CENTURY>>

**2001** The National Virtual Observatory project gets under way in the United States, developing methods for mining huge astronomical data sets.



2001 The US National Institutes of Health launches the Biomedical Informatics Research Network (BIRN), a grid of supercomputers designed to let multiple institutions share data.

2002 The Earth Simulator supercomputer comes online in Japan, performing more than 35 trillion calculations each second in its quest to model planetary processes.



**2005** The IBM Blue Gene family of computers is expanded to include Blue Brain, an effort to model neural behaviour in the neocortex — the most complex part of the brain.

2007 CERN's Large Hadron Collider in Switzerland, the world's largest particle accelerator, is slated to come online. The flood of data it delivers will demand more processing power than ever before.

Jacqueline Ruttimann

### <<BIRN